

WHAT IS CLAIMED IS:

1. A genetically-modified mammal capable of expressing at least one chimeric immunoglobulin gene comprising at least one detectable protein or peptide fused with a gene expressing an immunoglobulin component selected from the group consisting of the kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an immunoglobulin heavy chain, and any combination thereof, wherein antibodies secreted by immune cells of said genetically-modified mammal comprise said at least one detectable protein or peptide.
2. The genetically-modified mammal of claim 1 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide.
3. The genetically-modified mammal of claim 2 wherein a polynucleotide encoding said at least one detectable peptide or protein present at the C-terminus of the gene product of said fusion polynucleotide is located in exon G1.
4. The genetically-modified mammal of claim 1 wherein said at least one detectable peptide or protein is present at the C-terminus of the gene product of said fusion polynucleotide with a flexible linker peptide therebetween.

1 5. The genetically-modified mammal of claim 4 wherein a polynucleotide encoding said at
2 least one detectable peptide or protein present at the C-terminus of the gene product of
3 said fusion polynucleotide with a flexible linker therebetween is located in exon G1.

1 6. The genetically-modified mammal of claim 1 wherein said immunoglobulin heavy chain
2 gene is selected from the group consisting of IgG, IgM, IgD and IgA.

1 7. The genetically-modified mammal of claim 1 wherein an immunoglobulin molecule
2 secreted by immune cells of said genetically-modified mammal comprises at least one
detectable protein or peptide in the heavy chain of said immunoglobulin molecule.

8. The genetically-modified mammal of claim 1 wherein an immunoglobulin molecule
secreted by immune cells of said genetically-modified mammal comprises at least one
detectable protein or peptide in the light chain of said immunoglobulin molecule.

9. The genetically-modified mammal of claim 1 wherein an immunoglobulin molecule
secreted by immune cells of said genetically-modified mammal comprises at least one
detectable protein or peptide in the heavy chain and at least one detectable protein or
peptide in the light chain of said immunoglobulin molecule.

1 10. The genetically-modified mammal of claim 1 wherein at least one said detectable protein
2 or polypeptide is capable of quenching fluorescence.

1 11. The genetically-modified mammal of claim 1 wherein said at least one detectable protein
2 or peptide is an autofluorescent protein or peptide, a visibly-detectable protein or peptide,
3 an enzymatically active protein or peptide, a protein or peptide capable of interacting with
4 another molecule to produce a detectable product, or any combination thereof.

1 12. The genetically-modified mammal of claim 11 wherein said at least one detectable
2 protein is an autofluorescent protein or peptide.

1 13. The genetically-modified mammal of claim 11 wherein said autofluorescent protein or
2 peptide is selected from the group consisting of green fluorescent protein, red fluorescent
3 protein, and a fluorescent analog or fragment of any of the foregoing.

1 14. The genetically-modified mammal of claim 12 wherein said autofluorescent protein is
2 green fluorescent protein.

1 15. The genetically-modified mammal of claim 11 wherein said at least one detectable
2 protein is a combination of an autofluorescent protein or peptide and an enzymatically-
3 active protein or peptide.

1 16. The genetically-modified mammal of claim 15 wherein said at least one detectable
2 protein is a combination of green fluorescent protein and alkaline phosphatase.

1 17. An genetically-modified immune cell capable of expressing at least one chimeric
2 immunoglobulin gene comprising at least one detectable protein or peptide fused with a
3 gene expressing an immunoglobulin component selected from the group consisting of the
4 kappa immunoglobulin light chain, the lambda immunoglobulin light chain, an
5 immunoglobulin heavy chain, and any combination thereof, wherein antibodies secreted
6 by said genetically-modified immune cell comprise said at least one detectable protein or
7 peptide.

1 18. The genetically-modified immune cell of claim 17 wherein said at least one detectable
2 peptide or protein is present at the C-terminus of the gene product of said fusion
3 polynucleotide.

1 19. The genetically-modified immune cell of claim 18 wherein a polynucleotide encoding
2 said at least one detectable peptide or protein present at the C-terminus of the gene
3 product of said fusion polynucleotide is located in exon G1.

1 20. The genetically-modified immune cell of claim 17 wherein said at least one detectable
2 peptide or protein is present at the C-terminus of the gene product of said fusion
3 polynucleotide with a flexible linker peptide therebetween.

1 21. The genetically-modified immune cell of claim 20 wherein a polynucleotide encoding
2 said at least one detectable peptide or protein present at the C-terminus of the gene

product of said fusion polynucleotide with a flexible linker therebetween is located in
exon G1.

22. The genetically-modified immune cell of claim 17 wherein said immunoglobulin heavy
chain gene is selected from the group consisting of IgG, IgM, IgD and IgA.

23. The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule
secreted by said immune cell comprises at least one detectable protein or peptide in the
heavy chain of said immunoglobulin molecule.

24. The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule
secreted by said genetically-modified immune cells comprises at least one detectable
protein or peptide in the light chain of said immunoglobulin molecule.

25. The genetically-modified immune cell of claim 17 wherein an immunoglobulin molecule
secreted by said genetically-modified immune cells comprises at least one detectable
protein or peptide in the heavy chain and at least one detectable protein or peptide in the
light chain of said immunoglobulin molecule.

26. The genetically-modified immune cell of claim 17 wherein at least one said detectable
protein or polypeptide is capable of quenching fluorescence.

1 27. The genetically-modified immune cell of claim 17 wherein said at least one detectable
2 protein or peptide is an autofluorescent protein or peptide, a visibly-detectable protein or
3 peptide, an enzymatically active protein or peptide, a protein or peptide capable of
4 interacting with another molecule to produce a detectable product, or any combination
5 thereof.

1 28. The genetically-modified immune cell of claim 27 wherein said at least one detectable
2 protein is an autofluorescent protein or peptide.

1 29. The genetically-modified immune cell of claim 28 wherein said autofluorescent protein or
2 peptide is selected from the group consisting of green fluorescent protein, red fluorescent
3 protein, and a fluorescent analog or fragment of any of the foregoing.

1 30. The genetically-modified immune cell of claim 29 wherein said autofluorescent protein is
2 green fluorescent protein.

1 31. The genetically-modified immune cell of claim 27 wherein said at least one detectable
2 protein is a combination of an autofluorescent protein or peptide and an enzymatically-
3 active protein or peptide.

1 32. The genetically-modified immune cell of claim 31 wherein said at least one detectable
2 protein is a combination of green fluorescent protein and alkaline phosphatase.

1
2 33. A hybridoma comprising the genetically-modified immune cell of claim 17.

1 34. A chimeric, detectably-labeled immunoglobulin molecule comprising at least one
2 detectable protein or peptide fused with the kappa immunoglobulin light chain, the
3 lambda immunoglobulin light chain, an immunoglobulin heavy chain, or any combination
4 thereof.

1 35. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said at
least one detectable peptide or protein is present at the C-terminus of the gene product of
said fusion polynucleotide.

1 36. The chimeric, detectably-labeled immunoglobulin molecule of claim 35 wherein a
polynucleotide encoding said at least one detectable peptide or protein present at the C-
terminus of the gene product of said fusion polynucleotide is located in exon G1.

1 37. The chimeric, detectably-labeled immunoglobulin molecule of claim 35 wherein said at
2 least one detectable peptide or protein is present at the C-terminus of the gene product of
3 said fusion polynucleotide with a flexible linker peptide therebetween.

1 38. The chimeric, detectably-labeled immunoglobulin molecule of claim 37 wherein a
2 polynucleotide encoding said at least one detectable peptide or protein present at the C-
3 terminus of the gene product of said fusion polynucleotide with a flexible linker
4 therebetween is located in exon G1.

1 39. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said
2 immunoglobulin heavy chain gene is selected from the group consisting of IgG, IgM, IgD
3 and IgA.

40. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at
least one detectable protein or peptide in the heavy chain of said immunoglobulin
molecule.

41. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at
least one detectable protein or peptide in the light chain of said immunoglobulin
molecule.

1 42. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 comprising at
2 least one detectable protein or peptide in the heavy chain and at least one detectable
3 protein or peptide in the light chain of said immunoglobulin molecule.

1 43. The chimeric, detectably-labeled immunoglobulin molecule of claim 42 wherein at least
2 one said detectable protein or polypeptide is capable of quenching fluorescence.

1 44. The chimeric, detectably-labeled immunoglobulin molecule of claim 34 wherein said at
2 least one detectable protein or peptide is an autofluorescent protein or peptide, a visibly-
3 detectable protein or peptide, an enzymatically active protein or peptide, a protein or
4 peptide capable of interacting with another molecule to produce a detectable product, or
5 any combination thereof.

45. The chimeric, detectably-labeled immunoglobulin molecule of claim 44 wherein said at
least one detectable protein is an autofluorescent protein or peptide.

46. The chimeric, detectably-labeled immunoglobulin molecule of claim 45 wherein said
autofluorescent protein or peptide is selected from the group consisting of green
fluorescent protein, red fluorescent protein, and a fluorescent analog or fragment of any of
the foregoing.

1 47. The chimeric, detectably-labeled immunoglobulin molecule of claim 46 wherein said
2 autofluorescent protein is green fluorescent protein.

1 48. The chimeric, detectably-labeled immunoglobulin molecule of claim 44 wherein said at
2 least one detectable protein is a combination of an autofluorescent protein or peptide and
3 an enzymatically-active protein or peptide.

1 49. The chimeric, detectably-labeled immunoglobulin molecule of claim 48 wherein said at
2 least one detectable protein is a combination of green fluorescent protein and alkaline
3 phosphatase.

1 50. A method for producing a quantity of detectably-labelled polyclonal antibodies
2 comprising the steps of
3 a) providing a genetically-modified mammal in accordance with claim 1;
4 b) immunizing said genetically-modified mammal with a preselected immunogen,
5 wherein said genetically-modified mammal generates antibodies to said
6 immunogen, wherein antibodies secreted by immune cells of said genetically-
7 modified mammal comprise said at least one detectable protein or peptide; and
8 c) isolating said detectably-labelled antibodies from said genetically-modified
9 mammal.

1 51. A method for producing a quantity of detectably-labelled monoclonal antibodies
2 comprising the steps of
3 a) preparing a genetically-modified mammal in accordance with claim 1;
4 b) immunizing said genetically-modified mammal with a preselected immunogen,

- 5 wherein immune cells of said genetically-modified mammal generate antibodies
6 to said immunogen, wherein antibodies secreted by said immune cells comprise
7 said at least one detectable protein or peptide; and
- 8 c) immortalizing antibody-producing immune cells isolated from said genetically-
9 modified mammal;
- 10 d) selecting immortalized immune cells isolated from said genetically-modified
11 mammal that secrete antibodies specific to said immunogen; and
- 12 e) preparing a quantity of detectably-labeled monoclonal antibodies from said
13 selected immune cells.

52 A genetically-modified mammal capable of producing a detectably-labeled
immunoglobulin in response to immunization by an antigen, the genome of said mammal
comprising at least one fusion polynucleotide consisting of a polynucleotide sequence
encoding at least one detectable protein or peptide fused with a gene selected from the
group consisting of the kappa immunoglobulin light chain gene, the lambda
immunoglobulin light chain gene, an immunoglobulin heavy chain gene, and any
combination thereof, wherein antibodies secreted by immune cells of said genetically-
modified mammal comprise said at least one detectable protein or peptide.

1 53. A chimeric, detectably-labeled immunoglobulin molecule comprising at least one
2 fluorescent protein or peptide and at least one fluorescence-quenching protein or peptide
3 fused with a component of said immunoglobulin molecule independently selected from

4 the group consisting of the kappa immunoglobulin light chain, the lambda
5 immunoglobulin light chain, an immunoglobulin heavy chain, and any combination
6 thereof.

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